A longitudinal study of the relation of lead in blood to lead in air concentrations among battery workers

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Abstract
The relation between lead in air (PbA) and lead in blood (PbB), concentrations was investigated among 44 workers in five major operations in a United States high volume, lead acid battery plant. The study covered a 30 month period in which workers received frequent PbA and PbB determinations, workers remained in a single job, and PbA concentrations averaged below the US Occupational Safety and Health Administration (OSHA) permissible exposure limit of 50 $\mu g/m^3$. In both univariate and multivariable linear regressions, longitudinal analyses averaging PbA concentrations over the 30 month study period appeared superior to cross sectional analyses using only six month PbA averages to model PbB concentrations. The covariate adjusted coefficient (α value) for PbA (μ/m^3) in models of PbB ($\mu g/100$ g) was 1·14. This figure is strikingly higher than that reported in previous studies in the lead acid battery industry in all of which PbA concentrations were substantially higher than in the current study. Plausible explanations for the differences in α values include non-linearity of the PbA-PbB curve, a higher fraction of large size particulate associated with higher PbA concentrations, survivor bias among workers exposed to higher PbA concentrations, and the cross sectional designs of most previous studies. Despite previously reported problems with the model used by OSHA to predict PbA-PbB relations, the findings of this study are in good agreement with the predictions of that model.

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Lead is a human health hazard with a long history of industrial uses. When United States federal regulators set out to reduce lead exposure in the workplace in the mid-1970s, their decisions were based largely upon studies and models of exposure to lead in the battery industry. Since then, new production technologies have resulted in reductions in lead exposure in most major battery manufacturing plants.[1]

The US Occupational Safety and Health Administration (OSHA) choice of a permissible exposure limit for lead of 50 $\mu g/mg^3$ was determined largely by a model which predicted the distribution of workers' blood lead concentrations for a given air lead exposure.[2] This model was based on experimental data concerning the relation of lead absorption to lead particulate size and on a set of assumptions, without an empirical basis, regarding lead particulate size distributions in the lead battery industry.[3] We recently showed that this set of assumptions differed in important respects from empirical data received from the lead battery industry.[4] If the OSHA model were to be directly applied to the actual particle size distributions, significantly lower blood lead concentrations would be predicted for a given air lead exposure. None the less, many previous studies in the lead battery industry of the relation between total air lead (PbA) and blood lead (PbB) concentrations have been in rough agreement with the unmodified OSHA predictions.[5-10] These studies have usually considered only a limited number of covariates, however, and have not directly examined the relative contributions of various particulate size fractions to lead body burden. Also, most of these studies have been cross sectional in design. Other investigations have suggested that longitudinal study designs may be required to model accurately PbA-PbB relations.[11 12] Accurate modelling of PbA-PbB relations, particularly at air lead concentrations below the current standard is of concern in the light of recent reports of adverse health effects at increasingly lower blood lead concentrations.[13] These reports place a possible lowering of the current legal limits for worker blood lead concentrations and the associated air lead concentrations on the scientific and policy agenda.

We present here a study that investigated the relation between PbA and PbB concentrations in 44 lead acid battery workers in one United States plant who were followed up for 30 months with frequent PbA and PbB determinations. This plant used modern battery manufacturing technology and the PbA concentrations found were low (usually $< 30 \ \mu g/m^3$). Several potentially important covariates were considered including job category, seniority, age, ethnicity, sex, and smoking habit.

The 44 participants comprised workers at the plant with less than or equal to 22 years seniority. As described elsewhere,[14] the 24 workers at the plant with more than 22 years seniority were excluded from further analyses owing to the apparently strong influence of high PbA exposures in the distant past on current PbB concentrations.

This paper focuses on differences between cross sectional and longitudinal models of PbA-PbB relations and a comparison of the current results with previous observational and experimental studies. The results presented here form part of a larger study, which also examined the effect of inclusion of information on particulate size distributions on PbA-PbB models.[14]

Methods
The plant is located in an eastern United States urban area and was built in the 1940s. It was converted from older grid moulding production processes to expanded grid processes in 1977–8. The plant continued to use these modern production processes from the time of their installation through the entire study period. Details of the production process have been provided elsewhere.[14] The plant is an older "bay style" plant, having a high bay low bay roof structure with many windows. Tempered makeup air is provided only in cool weather. Batteries for starting car, truck, and boat engines are produced at the facility. Maximum battery production at the plant was reported to be 12 000 to 14 000 units per day.

Eight manufacturing operations (job categories) were initially evaluated for possible study because they offered the highest potential for worker lead exposure. (see bold bordered processes in the figure) Of these eight, five job categories were selected for study because four or more workers were assigned to each category and workers in these categories did not wear respirators. These five job categories selected were plate pasting, offbearing, encapsulation, stacking, and cast-on-strap.

Air lead (PbA) and blood lead (PbB) sampling programme
Historical (1980–8) PbA and PbB sampling and analysis in the plant met or exceeded the require-

ments of the OSHA lead standard.[2] A trained technician performed the PbA sampling on representative workers in each job category for at least seven continuous hours. No formal procedure was adopted for selecting workers to be sampled; however, attempts were made to sample most operator locations within each job category across all work shifts during a calendar year. Air sampling was performed by attaching a 37 mm cassette containing a $0.8 \ \mu m$ nominal pore size, mixed cellulose acetate filter to the lapel of the workers. The air sampling pumps, attached to the workers belts, were connected to the filter cassettes by rubber hose. A flow rate of 2 l/min was used. Pump calibrations were made using a 1 l bubble tube.

Venous blood samples for PbB measurements were collected by a registered nurse from all workers in the selected job categories on a frequent basis. Two to four samples were typically collected from each worker in any six month period.

A single analytical laboratory was used to analyse the PbA and PbB samples from 1980–5. Air sample filters were digested and then analysed by atomic absorption spectrophotometry. Concentrations of PbB were determined by delves cup techniques on a separate atomic absorption spectrophotometer. This laboratory was accredited by the American Industrial Hygiene Association (AIHA) and participated in the Centres for Disease Control (CDC) blood lead proficiency programme and was a proficiency analytical testing (PAT) programme approved for lead sample analysis. In 1986, a new laboratory was chosen to analyse samples for PbA and PbB concentrations.

DATA SELECTION
Records for PbA concentrations were reviewed for the years 1980 to the end of the third quarter of 1988 in the selected job categories. In linear regression analyses over the nearly nine year period, the average change in PbA concentration per year was small (from -0.39 to $0.89 \ \mu g/m^3$ per year across the five job categories).[14] Quarterly mean PbA concentrations and detailed regression results have been reported elsewhere.[4 14] The recessionary period for the car industry in the early 1980s resulted in many workers being on lay off or changing job categories. As a result, relative job category was stable only after the middle of 1983.

As a result of the above considerations, the period from the last half of 1983 (designated 1983b) to the end of the last half of 1985 (1985b) was selected for study. This resulted in a 30 month study period during which there were regular samples for the measurement of PbA and PbB concentrations collected from the study population, steady exposures, stability of worker job assignments and a single, approved laboratory performing all lead analyses.
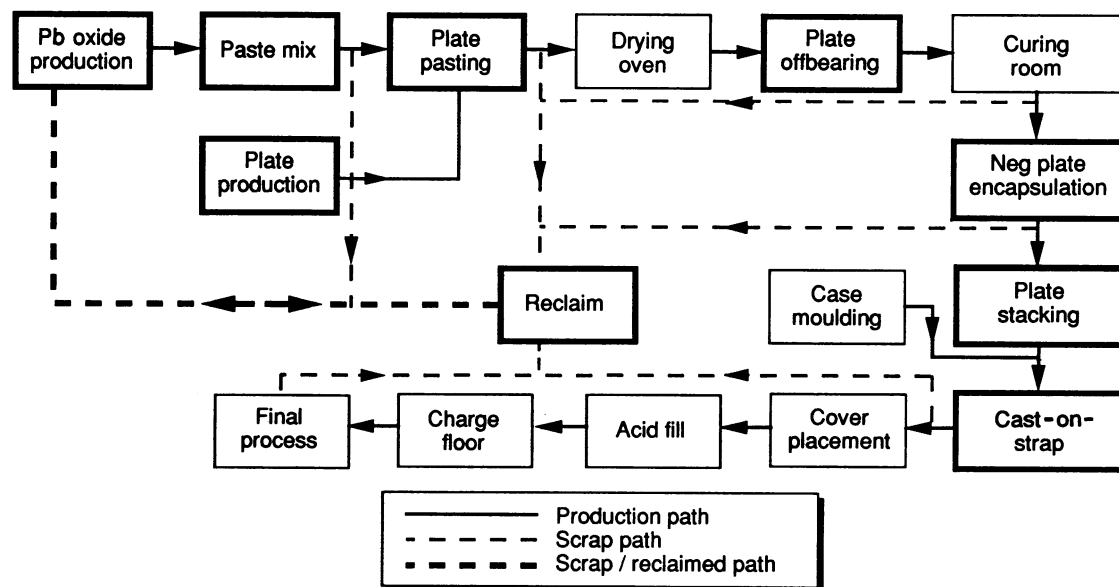
Battery manufacturing operation: expanded metal processes.

Workers' personnel and medical records were reviewed to obtain job assignment, work absence history, sex, ethnicity, cigarette smoking history, plant seniority, and age. Concentrations of PbA and PbB were collapsed into six month arithmetic means for the five periods of six months each from 1983b to 1985b. Each worker in the study had a PbB measurement for at least one sample for each of the six month periods, and most had two to four samples analysed during each period.

STUDY POPULATION

Workers selected for study were initially identified in a data base that included extensive data on job assignments. The records were updated on a weekly basis for change in work state that included job transfer and sick leave information. Workers missing from their job category for 40 or more weeks (10 months) during the time period July 1983 to the end of December 1985 were deleted from the analysis. Workers missing more than four weeks in the last six months of the study (second half of 1985) were also deleted.

Preliminary analyses of the worker population meeting this cohort definition showed an apparent effect of past PbA exposures on the PbB concentrations of workers with more than 22 years of plant seniority.[14] A significant PbA-PbB relation was not present in this subset of workers and appeared to be the result of past PbA concentrations well in excess of those measured after the change to expand metal grid

technologies. This lack of association was also present in a study of another battery plant from the same company.[14] As a result, this study's analysis of particle size was restricted to the subset of workers with less than or equal to 22 years of plant seniority.

STATISTICAL ANALYSES

Both univariate and multivariable linear regression models were examined cross sectionally and longitudinally. Cross sectional PbB-PbA regression analyses were performed by regressing the mean PbB concentration for the workers against the mean PbA concentration for the concurrent six month period. Longitudinal analyses were performed by regressing the mean PbB concentration for each of the five six month periods (1983b, 1984a, 1984b, 1985a, 1985b) against the arithmetic average of the six month PbA concentration means up to and including the concurrent six month study period. For example, the mean PbB concentration in 1984b was regressed against the arithmetic average of the PbA concentrations in 1983b, 1984a, and 1984b. Covariates initially considered for the multivariable analyses included seniority and indicator variables for job, sex, ethnicity, and smoking habit. The final longitudinal model (PbB concentration in 1985b against the average PbA concentration for the entire 30 month study period) was examined for covariates significant at $p < 0.15$. Three covariates, paste machine, black race, and smoking habit (coded as a no or yes variable), were retained in the model. The same three

covariates were included in all the other multivariable models for comparability of results across models.

Results

A total of 53 workers with less than or equal to 22 years of seniority worked in designated job categories during the study period. After assessment of work histories, nine of these workers were excluded from the study population because of absences resulting in the final study population of 44. None of these nine were excluded because of high blood lead measurements triggering OSHA required medical removal, but rather because of absence from their job categories as a result of elective transfers or personal sick leave not known to be related to exposure to lead.

Of the 44 final study subjects, 84% were men, 41% white (non-Hispanic), 9% Hispanic, 50% black, and 66% current smokers. Smokers in these groups were identified by review of questionnaires completed by workers and nurses at the time of periodic, roughly annual, physical examinations. No changes in worker smoking habits during the study period (for example,

starting or stopping) were found on these questionnaires. The mean age was 41·8 years; mean seniority was 12·8 years; mean total absences during the 30 month study and during the last half of 1985 were 1·4 and 0·05 months respectively. Thirteen worked in cast-on-strap, 14 in encapsulation, eight as offbearers, six on paste machine, and three as stackers. Mean blood lead concentrations for the last half of 1985 was 29·1 μg/100 g with a range of job specific means from 23·0 μg/100 g for encapsulation to 39·7 μg/100 g for paste machine.

Table 1 presents the job specific PbA and PbB concentrations for each of the five half year periods. A total of 219 air samples was collected over the 30 month period. Half year mean PbA concentrations varied from a low of 5 μg/m³ (stacker in 1985b) to a high of 33 μg/m³ (cast on strap in 1985a). The two and a half year job category means ranged from 11 to 19 μg/m³. Half year mean PbB concentrations varied from a low of 21 μg/100 g (stacker in 1985a) to a high of 40 μg/100 g (paste machine in 1985a). There were no statistically significant trends over time for either PbA or PbB in any of the five job categories.

Table 2 shows the results of the cross sectional and

Table 1   Worker PbA concentrations in μg/m³ and PbB concentrations in μg/100 g, by job category

Job category	PbA half year means (SD)											PbA mean†	PbB half year means (SD)					
	83b		No* 84a		No* 84b		No* 85a		No* 85b		No*		No‡	83b	84a	84b	85a	85b
Cast-on-strap	12 (7·7)	15	14 (17)	5	15 (9·2)	9	33 (22)	9	19 (15)	25	19	13	27 (8·5)	27 (7·4)	31 (9·0)	30 (8·4)	33 (8·9)
Encapsulation	10 (6·3)	16	15 (8·2)	12	13 (8·0)	13	10 (5·0)	8	6 (0·9)	6	11	14	24 (5·5)	22 (4·2)	24 (6·0)	22 (5·0)	23 (3·9)
Paste machine	10 (5·2)	8	26 (17)	7	16 (7·3)	5	20 (13)	9	15 (12)	3	17	6	31 (6·9)	33 (5·0)	36 (6·0)	37 (7·9)	40 (6·7)
Offbearer	17 (9·7)	10	13 (5·3)	8	14 (6·6)	10	8 (3·0)	3	16	1	14	8	25 (7·2)	23 (6·3)	25 (8·1)	27 (7·9)	28 (6·6)
Stacker	9 (4·4)	8	23	1	8 (4·5)	17	10 (2·6)	5	5 (2·8)	6	11	3	23 (7·2)	21 (6·7)	18 (7·2)	21 (4·0)	24 (6·5)

*Total number of personal breathing zone samples taken for each job category in each half year.
†Mean of five half year means.
‡Number of study subjects undergoing PbB sampling in each half year (all subjects provided samples in each half year).

Table 2   Cross sectional and longitudinal regression models of relations of PbA (μg/m³) to PbB (μg/100 g) among 44 battery workers

	Univariate models			Multivariable models									
	PbA			PbA		Current smoker		Paste machine		Black race		
Year	Coeff	p Value	Model r²	Coeff	p Value	Coeff	p Value	Coeff	p Value	Coeff	p Value	Model r²
					Cross sectional*							
1983b	−0·01	0·98	0·00	0·10	0·81	5·46	0·02	4·04	0·21	1·42	0·69	0·22
1984a	0·51	0·03	0·11	−0·37	0·33	5·73	0·005	11·23	0·03	0·34	0·85	0·38
1984b	2·35	0·0003	0·27	1·80	0·006	6·96	0·004	3·06	0·38	0·94	0·65	0·44
1985a	0·28	0·02	0·13	0·24	0·02	5·93	0·01	8·56	0·008	1·83	0·38	0·44
1985b	0·75	0·0005	0·26	0·59	0·0009	5·89	0·007	8·46	0·005	2·00	0·29	0·55
					Longitudinal†							
1983b	−0·01	0·98	0·00	0·10	0·81	5·46	0·02	4·04	0·21	1·42	0·69	0·22
1984a	1·22	0·03	0·11	0·64	0·42	5·83	0·005	9·97	0·03	0·70	0·69	0·37
1984b	2·42	0·005	0·18	0·86	0·61	7·11	0·007	4·18	0·57	1·01	0·66	0·33
1985a	1·43	0·0004	0·26	0·97	0·01	5·80	0·01	5·79	0·08	1·72	0·40	0·45
1985b	1·50	0·0001	0·36	1·14	0·0003	5·72	0·007	6·22	0·03	2·70	0·14	0·57

*Cross sectional models regress mean PbB concentration in each six month period against mean PbA concentration in the same period.
†Longitudinal models regress the mean PbB concentration in each six month period against the grand mean of the PbA concentrations from 1983b up to and including the same period.

longitudinal analyses. Each line in this table represents the outcomes of two separate regression models, one univariate and one multivariable. For the univariate analyses, the last four cross sectional models showed a statistically significant PbA-PbB association. However, the estimate of the coefficient appeared unstable and ranged from 0·51 in 1984a to 2·35 in 1984b. The last four longitudinal models also showed statistically significant PbA-PbB associations. In this case the coefficients appeared to converge to the final value of 1·50. Moreover, the p value decreased and the r² increased in each subsequent model. The r² of 0·36 in the final model compared favourably with the r² values in any of the cross sectional univariate models. In multivariable analyses, the last three cross sectional models showed a statistically significant PbA-PbB association. Again, the estimate of the PbA coefficient appeared unstable and ranged from 0·24 to 1·80. Only in the last two longitudinal analyses were there statistically

significant PbA-PbB associations with similar values for the PbA coefficient of 0·97 and 1·14 respectively. In all the multivariable models, being a current smoker was significantly positively associated with PbB. In most, work on the paste machine was also significantly, positively associated with PbB concentrations. Black race was of borderline significance only in the final longitudinal model. This model also evidenced the lowest p value for the PbA coefficient (0·0003) and the highest overall r² (0·57) of any of the multivariable models.

In interpreting the findings presented in table 2, it is important to note that 20 of the 44 workers studied were recalled to their jobs during the second half of 1983 after nine to 10 month layoffs. Most of the remaining workers would have changed jobs during this same period owing to seniority prerogatives. Thus, the initial poor PbA-PbB correlation in 1983b with subsequent improvement as seen in table 2 would not be unexpected.

Table 3   Summary of battery plant studies

Study	Year reported	No of workers	Study type	PbA* range (mcg/m³)	α†	Comments
Williams *et al*[6]	1969	39	Cross sectional	<5–300	0·20	Ten day study, mean of 10 PbA samples regressed against mean of duplicate PbB samples taken on one day—old process technology
King *et al*[8]	1979	19	Cross sectional	100–800	0·03	Three month study, mean of 10 PbA samples regressed against mean of three PbB samples collected at beginning, middle, and end of study—old process technology.
Gartside *et al*[7]	1982	132	Cross sectional	<10–350	0·54	Study performed during one year period; however, individual PbB result was regressed against a PbA result within 30 days of PbB sample—old process technology.
Bishop and Hill[9]	1983	233	Cross sectional	<10–200	0·04	Study performed over one year period, year mean PbB concentration was regressed against year mean PbA level—no information on operations—old process technology?
Bishop and Hill[9]	1983	?	Longitudinal	?	?	Study performed over about five and a half years, weighted monthly plant PbA concentrations were used in a time series analysis with monthly plant PbB concentrations, four of six plants from cross sectional study used—no information provided on operations or number of workers included—old process technology?
Chavalitnitikul *et al*[10]	1984	19	Cross sectional	2–165	0·16	Ten day study, mean of 10 PbA samples regressed against a single PbB sample collected during study—mostly old processes, possible newer encapsulation process as a single worker classified as "plate wrapper."
Matte *et al*[5]	1989	32	Cross sectional	30–5300	0·05	Single PbA measure regressed against single PbB measure—old process technology.
Current Study	1991	44	Longitudinal	5–33	1·14	Mean PbA concentration over three year period regressed against mean PbB concentrations during last half year of three year period—new process technology.

*Range provided by authors or determined by review of tables and figures in articles.
†Coefficeint of linear regression of PbB against PbA in mcg/100 g divided by mcg/m³.

Discussion

This study differs in several respects from most prior studies examining PbA-PbB relations. Firstly, it is a longitudinal design—that is, PbA concentrations averaged over a long period (30 months) were used to model PbB concentrations during the final six months of that three year period. Secondly, several potentially important covariates (smoking, specific job, ethnicity, and seniority) were controlled for in analyses. Thirdly, PbA concentrations were substantially lower than in most comparable studies in the lead acid battery industry. This is probably due to the fact that most of these previous studies are based on data collected before the promulgation of the OSHA lead standard and to the introduction of newer manufacturing technologies.

Table 3 summarises the design and findings of this and the major previous studies in the lead acid battery industry. All of the previous studies, except one by Bishop and Hill,[9] were cross sectional in design and examined workers using older manufacturing technologies (for example, grid moulding, manual or semiautomatic plate pasting, manual "plate dressing," and the use of individual plate separators). The "longitudinal" Bishop and Hill study did not provide information on which occupations were included, worker movements between jobs, or the air sampling scheme. In each of the previous studies for which information is available, the upper ranges of PbA exposures were substantially higher than in the current study. For each previous study, the value of the coefficient for PbA in a linear regression model of PbB, commonly known as α, is shown. The range of values of α for these studies (0·03 to 0·54) is strikingly lower than the covariate adjusted estimate of 1·14 or the unadjusted value of 1·50 for the current study.

There are at least four plausible explanations for the higher value of α found in the current study. Firstly, probable non-linearity of the PbA-PbB curve (the apparently decreasing values of α at higher PbA concentrations). This non-linearity has been reported in several previous studies[15-17] including experimental studies in which particulate size was controlled,[15 16] and has been discussed extensively in review articles by Hammond et al[18] and by Chamberlain.[19] Secondly, higher workplace PbA concentrations may generally be associated with a greater fraction of the total particulate being composed of larger particles, which would be expected to deposit predominantly in the ciliated airways and naso and oropharynx and ultimately to be ingested. Lead which is ingested is absorbed from the gastrointestinal tract with roughly 8% efficiency as compared with nearly 100% efficiency for lead depositing deep in the lung.[15 20-22] An association of higher PbA concentrations with larger particle sizes was assumed in the model used in the OSHA

Table 4   α Values (ratio PbB/PbA) of several experimental and environmental studies (from Chamberlain[19])

Study	α* (mean)	PbA (µg/m³)	Study type
Kehoe[15]	0·83	3·99 ± 2·40	Experimental
	0·65	24·0 ± 9·02	Experimental
Griffin et al[16]	1·45	10·4	Experimental
	1·8	3·1	Experimental
Azar et al[17]	1·81	0·1–6·1	Environmental
Tepper and Levin[24]	1·09	0·2–3·4	Environmental
Tsuchiya[25]	3·09	0·2–1·3	Environmental
Johnson[26]	1·11	0·6–6·3	Environmental
Current study	4·79†	5–33	Occupational

*α Values determined by either point estimates or regression analysis exposures represent a 24 hour/7 day week equivalent.
†α Value based on 40 hour work week adjusted to 24 hour/7 days per week equivalent (4·79 = 1·14 × 168/40).

standard to predict PbA-PbB relations.[3] Also, particulate size data previously reported from the current investigation found this type of distribution pattern.[4]

Thirdly, in the previous cross sectional studies that have PbA concentrations ranging well above the current OSHA standard of 50 µg/m³, a form of survivor bias may be reducing the apparent value of α. Those workers with high individual values of α would be the most likely to develop clinically apparent lead toxicity (or simply, pronounced increases in PbB concentrations) and be removed from the exposure on this basis reducing the mean α value among the remaining workers. Such an effect is unlikely to be operative to a significant degree at PbA concentrations below 50 µg/m³ as found in the current study.

Fourthly, most of the previous studies modelled PbB concentrations based on either concurrent PbA concentrations or on those collected during only a brief period before measurement of PbB concentrations. The data from the current study (table 2) and many earlier studies of lead elimination kinetics[10-12 23] suggest that incorporation of PbA exposures for several years before PbB measurement will improve predictions. Thus the failure of these previous studies to include longitudinal PbA data can be viewed as a form of non-differential misclassification of exposure tending to result in bias towards the null—that is, to decreased values of α. Also, most of these earlier studies have not included potentially important covariates in their models. Based on our current data, smoking habit and indicator variables for specific jobs appear particularly important. Data presented elsewhere[4] suggest that paste machine was a significant covariate because of the relatively higher proportion of small size particulate on this job as compared with the other jobs. Of course, inclusion of covariates could adjust the α value either upward or downward. In our data, their inclusion resulted in a reduction in α.

A comparison of the α value obtained in the current study with those obtained in experimental and environmental studies in which PbA concentrations were similar or lower than in the current study is informative. As seen in table 4 (adapted from Chamberlain[19]), the α value in the current study still appears higher than expected although it is somewhat closer to the range found in these studies as compared with the occupational studies shown in table 3. It should be noted that the validity of the 168/40 correction factor described in the footnote in table 4 is dependent on the assumption that the respiratory volume inhaled per unit time is the same during working and non-working periods. A higher respiratory rate during work periods may explain some part of the higher α value in the current study.

Finally, of interest is a comparison of the α for the current study with the α for the low exposed groups in the study by Williams *et al* included in table 3. The study[6] included two groups of workers from plastics departments as the "non-exposed" groups. In fact, the mean PbA exposures of 12 and 9 μg/m³ in plastics department A and B respectively are similar to the PbA exposures in the current study (table 1). Moreover, the α values of 0·93 and 1·46 found for workers in departments A and B respectively are remarkably similar to those of the current study.

If, in fact, the current study can be considered to be of a stronger design than most previous occupational studies, it is important to consider what the policy implications of our results may be. As we have described previously,[4] there appear to be several potential problems with the model chosen by OSHA to predict PbB concentrations based on PbA concentrations. Primary among these is that the assumptions of the model regarding particulate size distributions were not borne out by an empirical study of the lead acid battery industry. In a seniority range of three to 20 years, the OSHA model predicts PbB concentrations of approximately 28–32 μg/100 g for a PbA exposure of 11 μg/m³ and approximately 30–35 μg/100 g for a PbA exposure of 19 μg/m². Despite the potential concerns with the OSHA model, our results are in good agreement with the model predictions.

In summary, the current study is notable, firstly, for showing differences in the modelled PbA-PbB relations when cross sectional analyses are compared with longitudinal analyses based on three years of PbA measures (table 2). The greater stability of the longitudinal analyses suggests that, at least in situations such as the current study where individual PbA exposures are known to have changed dramatically just before the study time frame, the use of PbA exposure data measured over several years is critical to accurate predictions of PbB concentrations. This study is also notable for showing a surprisingly high value of α, even in view of the relatively low PbA concentrations. Notwithstanding this and some potential problems with the model used by OSHA in the lead standard, our data are in substantial agreement with the OSHA model predictions.

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